

Table of Contents

1	Introduction	7
1.1	Purpose and Scope	7
1.2	Key Considerations.....	7
2	Regulatory Considerations	9
2.1	RRD Requirements.....	9
2.2	Documentation Requirements	10
3	Industry Trend Considerations	13
3.1	Risk-Based Monitoring and Virtual Monitoring.....	13
3.2	Depot Monitoring versus CRA Monitoring.....	13
3.3	Direct-To-Patient Logistics and Decentralized Trials.....	14
3.4	Technology.....	14
3.5	Mergers and Acquisitions.....	15
3.6	Product Type.....	15
4	Product Considerations.....	17
4.1	Non-Solid Materials.....	17
4.2	Devices	17
4.3	Expired Materials	18
4.4	Hazardous Materials	18
4.5	Biologic Materials and Waste.....	18
4.6	Controlled Substances.....	19
4.7	Radiolabeled Materials	19
4.8	Materials with Multiple Special Characteristics	19
4.9	Packaging	20
5	Trial Conduct Considerations	21
5.1	Reconciliation Measures.....	21
5.2	Site Documentation.....	21
5.3	Objective Compliance Measures	22
5.4	Site Qualification	22
5.5	Retention Policies	22
6	Common RRD Approaches	23
6.1	Centralized: Return Everything to a Sponsor-defined Central Depot	23
6.2	Decentralized: Return Everything to a Local (e.g., In-Country) Destruction Facility	23
6.3	Decentralized: Return Nothing – Reconcile and Destroy at Site	24

7	Quality Considerations	25
7.1	GMP or GCP	25
7.2	QMS Jurisdiction	25
7.3	Setting Policy	27
7.4	Setting Standard Operating Procedures	28
7.5	Protocol and Pharmacy Manuals	29
7.6	Defining RACI	30
7.7	Change Management	30
7.8	Documentation	31
7.9	Due Diligence Investigations	32
7.10	Metrics and Quality Thresholds	32
7.11	Managing Discrepancies	33
7.12	Resolution of Discrepancies	39
8	Logistics Considerations	43
8.1	Return Exports	43
8.2	Direct-to-Patient	43
8.3	RRD Process Exemptions	44
8.4	Transfer of Ownership	44
9	Technology Considerations	45
9.1	Use of IRT For RRD	46
9.2	Use of Technology Pitfalls	46
10	Timeline Considerations	47
11	Appendix 1 – References	49
12	Appendix 2 – Glossary	51
12.1	Acronyms and Abbreviations	51
12.2	Definitions	52